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# POLICOSANOL: NATURAL WAX COMPONENT WITH POTENT HEALTH BENEFITS

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## ABSTRACT

Policosanol is a mixture of higher primary alcohols isolated from sugarcane wax, bees wax, rice bran, broccoli, spinach, oats and alfa-alfa with octacosanol as the main component. Policosanol has antioxidative, lipid lowering, antithrombotic effects and provides protection against free radical associated diseases. It seems a promising phytochemical alternative to classic lipid lowering drugs for the patients who although in the dire need of lipid lowering treatment, are reluctant to use chemically derived drugs and would gladly welcome a natural and efficient alternative. The review gives a brief account of the composition, bioactive components, their biochemical roles and therapeutic characteristics. An attempt has been made to include the available literature on the effectiveness of policosanol in the management of chronic diseases.

**KEYWORDS:** Policosanol, Sugarcane Wax, Hypocholesterolemic, Oxidative Stress, Antioxidant

## INTRODUCTION

Sugarcane *(Saccharum officinarum L)* popularly known as *noble cane* is one of the important industrial crops of the world. Besides a source of sugar production, its roots and stems are used as medicine in Ayurveda to treat skin and urinary tract infections as well as bronchitis, heart conditions, loss of milk production, cough, anaemia, constipation, jaundice and low blood pressure and general debility (Kadam et al., 2008).

White and black wax that adheres to the surface of raw sugarcane assists the plant in minimizing water evaporation, insect attack and reducing disease. It is a source of long chain carbohydrates with OH or CHO radical (Tamaki et al., 2003). In addition to wax esters, plant waxes and honey comb wax contains a variety of hydrophobic compounds that include non esterified very long chain hydrocarbons, alcohols, aldehydes and acids. However, few plants also contain a variety of branched lipids, secondary alcohols, diols, ketones and other metabolites (Kolattukudy, 1976; Bianchi, 1995).

Policosanol is a natural mixture of aliphatic primary alcohols found in waxes in plants such as sugarcane wax, bees wax, rice bran, broccoli, spinach, oats and alfa-alfa and is isolated by hydrolytic cleavage and subsequent purification. The main source of commercial policosanol is sugarcane wax either saponified or obtained by supercritical fluid extraction. The latter contains 50-72% of alcohols, acids and aldehydes. The chemical formula of policosanol is $CH_3$-($CH_2$)n-$CH_2OH$ with chain length varying from 24 to 34 carbon atoms. These high molecular weight alcohols possess antioxidant properties (Noa, 2002) and hypocholesterolemic properties (Tamaki et al., 2003).

## COMPOSITION

Its main components are octacosanol (64.5%) followed by tria contanol (12.8%) and hexacosanol (6.3%), while the other alcohols tetracosanol (0.7%), heptasanol (0.7%), nonacosanol (0.8%), dotriaconatonol (5.4%) and tetratriacontanol (0.9%) are minor components (Arruzazabala et al., 1997). Besides these, it also contains very long chain aliphatic alkanes, fatty aldehydes and fatty acids.

**Table1: Relative Composition of Policosanols Obtained from Different Sources**

| Policosanol | | Rice Bran Wax | Sugarcane Wax |
|---|---|---|---|
| Eicosanol | $C_{20}$ | - | - |
| Heneicosanol | $C_{21}$ | - | - |
| Docosanol | $C_{22}$ | 1.1 | - |
| Tricosanol | $C_{23}$ | - | - |
| Tetracosanol | $C_{24}$ | 11.6 | 0.7 |
| Pentacosanol | $C_{25}$ | - | - |
| Hexacosanol | $C_{26}$ | 10.6 | 8.0 |
| Heptacosanol | $C_{27}$ | - | 3.5 |
| Octacosanol | $C_{28}$ | 20.2 | 66.0 |
| Nonacosanol | $C_{29}$ | - | 0.8 |
| Triacontanol | $C_{30}$ | 30.1 | 13.5 |
| Dotriacontanol | $C_{32}$ | 16.8 | 6.0 |
| Tetratriacontanol | $C_{34}$ | 8.0 | 1.5 |
| Hexatriacontanol | $C_{36}$ | 1.4 | - |

**Source:** Stuchik and Zak, (2002)

## BIOACTIVE COMPONENTS

### Octacosanol

Octacosanol ($C_{28}H_{58}O$) is a 28 carbon, long-chain saturated primary alcohol. It is the most prominent member of the policosanol family (molecular weight 410.74) and popularized as an active ingredient in wheat germ oil. It is also found in spinach and sugarcane wax. Octacosanol is also known as l-octacosanol, n-octacosanol and octacosyl alcohol. It has the following chemical formula:

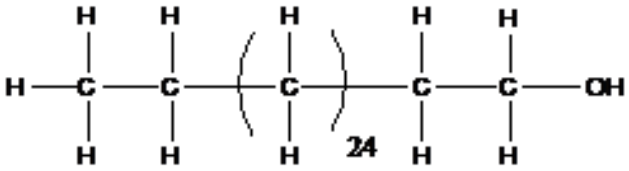


**Figure1: Structure of Octacosanol**

It is a solid waxy substance that is insoluble in water. Octacosanol containing wax is black and is present at the base of the mature cane after harvesting. Its proportion to other aliphatic alcohols in the policosanol profile varies with the source of the wax. For instance, sugarcane wax contains ≈ 60-70% octacosanol while rice bran wax contains 17.5%.

### Absorption and Distribution

A study reported that when small amounts of [$^{14}$C]-octacosanol was administered to rats through a stomach tube with a vehicle of tricaporyl glycerol, about half the dose was metabolized during the following week where as a third was excreted in the faeces (Kabir and Kimura, 1993). The highest concentration in plasma was observed in one hour after the

dose was administered. Liver, brown adipose and white adipose accumulated more than 1% of the administered dose per gram, whereas the concentrations of octacosanol in spleen, kidney, heart, lung, brain and muscle remained less than 0.4% of the dose (Hargrove et al., 2004).

Another study demonstrated that octacosanoic acid is formed after incubation of fibroblast cultures with (3) H-octacosanol and after oral dosing with policosanol to rats. In addition, shortened saturated (myristic, palmitic and stearic) and unsaturated (oleic, palmitoleic) fatty acids were also formed after oral dosing with policosanol to monkeys. The study suggested that octacosanol metabolism is linked to fatty acid metabolism via beta-oxidation.

**Biochemical Role**

Octacosanol have been reported to have many beneficial attributes in both animals and humans as it affects lipid metabolism, (Kato et al., 1995), increases the size of testes and seminal vesicles, improves motor endurance and physical exertion (Shimura et al., 1987). A study evaluated the effects of octacosanol on running performance and related biochemical parameters in exercise-trained rats run to exhaustion on a treadmill. The results suggested that the ergogenic properties of octacosanol include the sparing of muscle glycogen stores and increases in the oxidative capacity in the muscle of exercise-trained rats (Kim et al., 2003).

Furthermore, it is also effective in Parkinson's disease (Snider, 1984; Morris et al., 1986) and osteoporosis (Tamaki et al., 2003). However, the mechanism by which octacosanol acts in these specific diseases is by and large unknown.

**Triaconatanol**

Triaconatanol ($C_{30}H_{62}O$) is a linear saturated fatty alcohol and is also known as myricyl alcohol. It is found in plant cuticle wax and in bees wax. Its application to seedlings and growing plants increases growth rate and fruit yield.

The biologic activity of tetracosanol (24C) known as lignoceryl alcohal and hexacosanol (26C), also called ceryl alcohol, are poorly understood.

## HEALTH BENEFITS OF POLICOSANOL

**Ant oxidative Effects**

Studies have shown that policosanols are able to inhibit lipid peroxidation in experimental models as well as in human beings and have a beneficial effect against free radical associated chronic diseases. A study evaluated the antioxidant activity of policosanol on rat liver microsomes and concluded that when policosanols were administered orally (100 and 250mg/kg/day) for up to 4 weeks, there was partial prevention of rat microsomal lipid peroxidation *in vitro* and *in vivo* and copper induced lipoprotein peroxidation *in vitro*. (Fraga et al., 1997). Complementary to these results Menendez et al., (1999) demonstrated that oral treatment of rats with policosanol at 250-500mg/kg/day over a 4 week period resulted in increased protection of lipoprotein fractions against lipid peroxidation in the lipid as well as in protein moiety. Menendez et al., (2000a) further demonstrated that when policosanol is administered at 5 and 10 mg/day decreased the susceptibility of LDL to lipid peroxidation *in vitro*. Another study conducted on hypercholesterolemic patients demonstrated that policosanols (5mg/day) not only lowered total cholesterol, LDL-C, atherogenic indices and increased HDL-C but also significantly decreased the susceptibility of LDL to copper ion- induced lipid peroxidation in vitro (Menendez et al., 2000b). Similarly, in a study designed to investigate the effect of policosanols administered at 50mg/day

for 12 weeks on lipid peroxidation in the elderly. It was noted that the mixture significantly reduced the susceptibility of non fractioned plasma samples to copper mediated lipid peroxidation (Menendez et al., 2001). Thus, it indicates that policosanols may offer some protection against free radical associated diseases.

**Anti Thrombotic Effects and Cardiovascular Diseases**

Antithrombotic effect of policosanols has been demonstrated in several animal species including rabbits and other rodents. Specifically, policosanols have shown to exhibit effects on platelet activation, endothelium turnover and foam cell formation (Varady et al., 2003).

In a study, policosanol administered orally to rats at 5 to 20mg/kg were shown to inhibit collagen induced decreases in platelet counts in a dose dependent manner suggesting an *in vivo* antiaggretory effect. In addition, policosanols administered at a single dose of 25mg/kg were able to inhibit the formation of thromboxane $A_2$ ($TxA_2$, a potent platelet aggretory agent in both human and nonhuman species) (Arruzazabala et al., 1993a). Furthermore, when policosanols were administered orally (25, 50, 200mg/kg/day) to Mongolian gerbils, not only reduced $TxA_2$ levels but also increased $PgI_2$ levels in blood at a level of 200mg/kg/day (Arruzazabala et al., 1993b). Similarly, Arruzazabala et al., (1998) investigated the antithrombotic effect of policosanols in type II hypercholesterolemic individuals. The results revealed that policosanols (10mg/day) significantly inhibited platelet aggregation induced by arachiodonic acid and collagen after 30 days of treatment. Thus, it appears that policosanols may have antithrombotic effect not only in healthy individuals but also in those with abnormal lipid profiles.

Varady et al., (2003) suggested that policosanols at 200mg/kg/day may protect against cerebral ischemia by reducing the$TxA_2/PgI_2$ ratio. In a study policosanols administered at doses of 2.5mg/kg/day and 25mg/kg/day were shown to significantly reduce the formation of foam cells within the granulomas and the number of atherosclerotic lesions of the treated animals (Noa et al., 1996). Furthermore, Noa et al., (1997) reported that oral administration of policosanols (25mg/kg/day) in rats resulted in a significant protection of the endothelial cell lining against the desquamating effects of citrate. A similar reduction in the number of circulating endothelial cells was noted in spontaneously hypertensive rats after the administration of policosanols at a dose of 5mg/kg/day. Furthermore, a comparison between groups revealed a lower frequency of aortic lesion in policosanol treated animals than in controls suggesting a protective effect of policosanols on the vascular endothelium. A study examined the effects of long term lipid lowering therapy with policosanol on the clinical evolution and exercise-ECG testing performance of coronary heart disease patients concluded that policosanol treated CHD patients' improved clinical evolution and exercise-ECG responses owing to the amelioration of myocardial ischemia even more than when administered with asprin (Stusser et al., 1998).

**Hypocholesterolemic Effects**

The origin of research into cholesterol lowering effects of policosanol dates to 1972 when Japanese researcher Dr. Hiroko Sho demonstrated that rats fed black (raw) sugar showed significantly lower cholesterol and triglyceride levels than those fed on (white) refined sugar. Further, the same worker showed later that by feeding corn starch, sugars (black and white) and sugars supplemented with tocopherol also indicated that black sugar lowered serum cholesterol and triglyceride levels but the lowering factor in black sugar was found to be other than tocopherol. Subsequently, he identified the dominant components in sugar cane rind, wax and fatty alcohols and showed that these substances reduced cholesterol in the serum and liver of rats (Sho et al., 1981; 1984).

Menendez et al., (1994) demonstrated that when human lung fibroblasts were incubated in the presence of policosanols for 48hours, the incubation of $^{3}$H-water into the cholesterol was decreased and the uptake of $^{14}$C into cholesterol was decreased from the $^{14}$C-acetate but not from the $^{14}$C-mavelonate. The finding suggests that policosanols could possibly suppress the action of HMG-CoA reductase, a key enzyme in the first step of cholesterol biosynthesis. In addition, investigators noted that LDL binding, internalization and degradation were significantly increased after policosanol treatment. A study conducted by Torres et al., (1995) concluded that policosanol (10mg/day) has cholesterol lowering effects in patients with hyperlipoproteinemia and controlled NIDDM.

Studies have also shown that policosanols lower cholesterol levels by reducing cholesterol biosynthesis and enhancing LDL receptor mediated clearance. Menendez et al., (1997) administered policosanols orally at a dosage of 50mg/kg/day to casein induced hypercholesterolemic rabbits for a period of 30 days. Incorporation of $^{3}$H-water into the hepatic sterols was significantly depressed while clearance of low density lipoprotein (LDL) cholesterol was significantly improved. Varady et al., (2003) suggested that the administration of policosanols inhibit cholesterol biosynthesis and enhance LDL decatabolism. Ng et al., (2005) reported that greater excretion of acidic sterols was associated with the consumption of policosanol. Haim et al., 2012, demonstrated that esterification of policosanol with oleic acid enhances policosanol bioavailability, and significantly improves the serum lipid profile in normocholesterolemic rats in association with the inactivation of HMG-CoA red controlling cholesterogenesis.

In several double blind randomized placebo controlled clinical trials, policosanol has been shown to reduce total cholesterol, reduce LDL cholesterol and raise HDL cholesterol level with no significant change in triglyceride levels (Castano et al., 1995a; 1995b; 1996; 1997; 1998; Mas et al., 1999). Similarly, Gamez et al., (2005) investigated the effect of concurrent therapy with policosanol and omega-3 fatty acid on lipid profile and platelet aggregation in rabbits and suggested that the combined therapy could be useful for regulating lipid profile and inhibiting platelet aggregation. A study compared the efficacy and safety of plant sterols, stanols and policosanol in the treatment of coronary heart disease and concluded that plant sterols, stanols and policosanol are well tolerated and safe, however, policosanol is more effective than plant sterols and stanols for LDL level reduction and more favorably alters the lipid profile approaching antilipidemic drug efficacy (Chen et al., 2005).

**Comparison of Policosanol and other Lipid Lowering Therapies**

Although several effective drugs such as statins, nicotinic acid, ionic exchange resins, fibrates and prubocol have been developed and marketed for the- management of dyslipidemia, data indicate that these agents are associated with certain long term side effects namely hepatotoxicity and myopathy (Varady et al., 2003).

For this reason, comparing the efficacy of policosanols as lipid lowering agents with no side effects to such therapies is of special interest. Berthold and Berthold., (2002), stated that policosanol seems to be a very promising phytochemical alternative to classic lipid-lowering agents such as statins. Studies indicate that policosanol has performed equal to or better than lovastatin, prubucol, simvastatin and acipimox in type II hyper cholesterolemia with fewer side effects (Janikula, 2002). A study in patients with NIDDM comparing policosanol and lovastatin showed that policosanols at 10mg/day produce more advantageous changes in HDL cholesterol and exhibit better safety and tolerability than lovastatin at 20mg/day (Crespo et al., 1999). When compared at the same dosage (10mg/day), policosanol showed a more favourable effect on lipid profiles than pravastatin. In addition, policosanols but not pravastatin increased HDL (Castano et al., 1999). When policosanols (10mg/day) were compared with another lipid lowering agent, Acipimox (750mg/day), a nicotinic acid

derivative, both therapies significantly reduced total and LDL-C levels after 8 weeks of treatment (Alcocer et al., 1999). However, the policosanol therapy led to a larger decrease in both the LDL: HDL and TC: HDL ratios.

## TOXICITY EVALUATION

Since policosanols are effective only when used on a repeated basis, therefore its toxic evaluation related to its chronic use is of utmost importance. Aleman et al., (1994) demonstrated that policosanol administered to rats at 50 to 500 mg/kg/day for 12 months revealed no toxicity in terms of clinical observation as well as blood biochemistry. Likewise, *in vitro* and *in vivo* mutagenicity studies showed that policosanols were not related to any genotoxic effects on somatic or germinal cells (Rendon et al., 1992). Results of long term clinical trials support its safety and tolerability (Pons et al., 1992).

Another study evaluated peri and post-natal toxicity of policosanol in rats by administering it orally at a dose level of 0 (control), 5, 50, 500mg/kg/day, from day 15 of pregnancy to day 21 after parturition. The study confirmed that there were no adverse effects on post-natal growth, behaviour and reproductive ability of F1 pups. Furthermore, the sensorial development of F2 pups was also normal (Rodriguez and Garcia, 1998).

## CONCLUSIONS

An intriguing characteristic of policosanol is its natural source. Besides this, it has a nutritional perspective in addition to pharmaceutical perspective. It makes policosanol an attractive alternative for a large number of patients who, although in the dire need of lipid lowering treatment, are reluctant to use chemically derived drugs and would gladly welcome a natural and efficient alternative.

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